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Type 2 myocardial infarction.

The advent of the measurement of cardiac troponins cardiac troponin T and cardiac troponin I offered the clinician and the laboratory a new tool to detect myocardial injury in patients suspected of acute myocardial infarction. The new tests were both more sensitive and specific than the biomarkers they replaced due to their absolute specificity for myocardial injury. The ability to predict an adverse prognosis in patients previously considered to have unstable angina and the ability to guide therapy led to their widespread adoption and ultimately to the redefinition of acute myocardial infarction to incorporate troponin measurement. The original redefinition of myocardial infarction does not contain any mention of subtypes of acute myocardial infarction (AMI)[1]. It only recommends the use of cardiac troponin as the preferred biomarker in the presence of other features which clinicians recognise as being indicative of myocardial ischaemia. The first appearance of the fivefold classification of AMI appears in the universal definition of myocardial infarction and has been elaborated subsequently through the two recent redefinitions[2].

The universal definition of myocardial infarction (MI) provides 5 subtypes of acute myocardial infarction. Type 1 is what is generally understood to be a “heart attack”. Type 3 is the diagnosis when there is no biomarker information available. Type 4a (post percutaneous intervention MI) and type 5 MI are arbitrary and constructs judged by biomarker elevation alone where a decision threshold has been selected to delineate whether significant or insignificant myocardial injury has occurred. Type 4b MI has a more rational pathophysiological basis as it is a combination of a cardiac troponin above the 99th percentile plus angiographic evidence of a thrombus. This leaves Type 2 MI. What is type 2 MI and why does it exist?

In order to appreciate the concept of type 2 MI it is necessary to consider the origins of cardiac troponin testing and the subsequent evolution from the initial assays to the current generation of high sensitivity assays able to reliably measure troponin levels even in those considered to be entirely healthy. The original troponin assays were relatively insensitive and were optimised to give equivalent performance to a diagnostic classification based on the old WHO definition of acute myocardial infarction. This resulted in the use of very high cut-offs which gave the assays apparently excellent specificity and permitted a dichotomous classification of patients into acute myocardial infarction or not. At the time of introduction the assays were considerably more expensive than the conventional approach based on “cardiac enzymes”. Hence originally only a single estimation was recommended at the 12 hour time point. Since then there has been progressive improvement in assay sensitivity and a clinical realisation that low-level troponin elevations in patients presenting with acute coronary syndromes (ACS) have diagnostic and prognostic significance. The progressive improvement in assay sensitivity has also broadened the number of conditions in which troponin elevation can be detected[2]. Elevation of troponin in these patients groups has been found to indicate an adverse prognosis no matter what the clinical situation. Type 2 myocardial infarction has been used as the diagnostic label that encompasses this group of patients. But which ones truly are Type 2 MI?

Type 2 myocardial infarction is considered to have taken place

“in instances of myocardial injury with necrosis were a condition other than CAD contributes to an imbalance between myocardial oxygen supply and/or demand e.g. coronary endothelial dysfunction, coronary artery spasm, coronary embolism, tachy-/brady-arrhythmias, anaemia, respiratory failure, hypertension, and hypertension with or without LVH.[2]”

The problem with this definition is that it is subjective. Objective diagnostic criteria have not been supplied. The diagnosis of type 2 myocardial infarction has been examined in a large Swedish registry study by Baron et al published in Heart. The series is large. 20,138 hospitalisations with a diagnosis of acute myocardial infarction were examined. The majority of cases (88.5%) were classified as type 1 MI with 7.1% classified type 2 MI. The diagnosis of type 2 MI was made by the local clinicians and submitted to the registry. It was noted that the number of reported cases of type 2 MI varied considerably between the reporting sites with a range from 0.2-13% (10th to 90th percentile) with a median 6.7%. This, in itself, illustrates the problems with making the diagnosis of type 2 MI.

It is worth comparing and contrasting the findings in this multicentre registry with that of a large and well documented single centre study performed in Denmark[3]. In the Danish study the number of patients with type 2 MI was higher (24.8%). There are marked similarities between the populations with type 2 MI. In both series the patients were older, had a previous history of diabetes, heart failure and stroke. The Danish cohort had no difference in a history of previous MI or revascularisation between type 1 and type 2 MI in contrast to the Swedish study. In addition, the Danish cohort showed no difference in the prescription of cardioprotective agents and statins prior to admission whereas the Swedish cohort showed a much higher incidence of prescription of these agents in the type 2 MI group. In both series type 2 MI was associated with lower rates of coronary angiography or revascularisation procedures and treatment with cardioprotective agents and statins in hospital and on discharge. The range of discharge diagnoses associated with type 2 myocardial infarction was similar between the two series. In both series the magnitude of troponin elevation was less in type 2 than type 1 MI although only the Danish study used a high sensitivity troponin assay for all patients. However, the mortality reported by the two series is different. In the Danish study type 2 MI was a significant predictor of an adverse outcome using multi variable regression analysis. The Swedish study the crude one year mortality was higher in type 2 MI than type 1 MI on univariate analysis but after adjustment background characteristics, treatments and clustering by treating hospitals the difference in one year mortality was attenuated and did not reach statistical significance.

Both of these studies are well performed but have produced mortality conclusions pointing in different directions. How can we square this circle? Does the difference between the two studies represent the problem of making a final diagnosis of type 2 MI, a difference in troponin assays or is there a deeper more fundamental problem? It has been demonstrated that using a lower detection limit for troponin in a population admitted with suspected ACS results in more interventions with improvement in mortality[4]. This study did not distinguish between type 1 and type 2 MI. It is clear that troponin elevation outside of the acute coronary syndrome population has diagnostic and prognostic significance though as a marker of myocardial injury rather than as a test of acute myocardial infarction[5]. There is clearly a need for further research and discussion of the concept of type 2 MI.

The definition of type 2 MI was debated at the European Society of Cardiology annual congress with a promise that further redefinition of was being considered. Further debate and discussion of this topic is required. Perhaps we should do away with term type 2 MI entirely and revert back to the original redefinition acknowledging that troponin elevations occur in other conditions than AMI (Secondary Ischaemic Myocardial Injury). These troponin elevations indicate that the patient has a condition which has caused, or is causing, myocardial injury. Such patients need assessment and care but not necessarily by a cardiologist and not necessarily as an inpatient. Troponin elevation needs to be seen as a useful diagnostic tool with excellent negative predictive value but it is not the sole arbiter of AMI and must be combined with the clinical assessment the patient.

References

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